

In re Application of: Michal DANIELY et al
Serial No.: 10/771,440
Filed: February 5, 2004
Office Action Mailing Date: April 29, 2010

Examiner: DUFFY Bradley
Group Art Unit: 1643
Attorney Docket: 26003
Confirmation No.: 3178

In the Claims:

1-71. (Cancelled)

72. (Currently Amended) A method of identifying transitional cell carcinoma cells in a voided urine sample comprising:

(a) staining nucleated cells of the voided urine sample using a stain selected from the group consisting of May-Grünwald-Giemsa, Giemsa, Papanicolaou and Hematoxylin-Eosin to thereby obtain stained nucleated cells, and subsequently;

(b) imaging said stained nucleated cells resultant of step (a) so as to obtain images of said stained nucleated cells, and subsequently;

(c) analyzing a nucleus to cytoplasm ratio in transitional epithelial cells identifying by said stain in said images of step (b) and identifying a single cell having a morphological abnormality which comprises a high nucleus to cytoplasm (N/C) ratio as compared to a transitional epithelial cell with a normal morphology, said morphological abnormality which indicates that said single cell is suspicious as being a transitional cell carcinoma (TCC) cell, and subsequently;

(d) staining said stained nucleated cells resultant of step (a) using fluorescent *in situ* hybridization (FISH) to thereby obtain nucleated cells stained with FISH, and subsequently;

(e) imaging said nucleated cells stained with FISH resultant of step (d) so as to obtain images of said nucleated cells stained with FISH, and subsequently;

(f) identifying by said FISH in said images of step (e) a chromosomal abnormality in the same said single cell identified in step (e) having said morphological abnormality, suspicious as being said transitional cell carcinoma (TCC) cell wherein said chromosomal abnormality indicates that said single cell is a transitional cell carcinoma (TCC) cell;

wherein presence of said morphological abnormality nucleus to cytoplasm ratio and said chromosomal abnormality in the same said single cell confirms that said same single cell is a transitional cell carcinoma (TCC) cell,

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thereby identifying the transitional cell carcinoma cells in the urine sample.

73. (Currently Amended) A method of diagnosing bladder cancer in a subject, the method comprising:

- (a) obtaining a voided urine sample from the subject;
- (b) identifying transitional cell carcinoma cells according to the method of claim 72, staining nucleated cells of said urine sample using a stain selected from the group consisting of May Grünwald Giemsa, Giemsa, Papanicolaou and Hematoxylin Eosin to thereby obtain stained nucleated cells, and subsequently;
 - (c) imaging said stained nucleated cells resultant of step (b) so as to obtain images of said stained nucleated cells, and subsequently;
 - (d) identifying by said stain in said images of step (c) a single cell having a morphological abnormality which indicates that said single cell is suspicious as a transitional cell carcinoma (TCC) cell, and subsequently;
 - (e) staining said stained nucleated cells resultant of step (b) using fluorescent *in situ* hybridization (FISH) to thereby obtain nucleated cells stained with FISH, and subsequently;
 - (f) imaging said nucleated cells stained with FISH resultant of step (e) so as to obtain images of said nucleated cells stained with FISH; and subsequently;
 - (g) identifying by said FISH in said images of step (f) a chromosomal abnormality in the same said single cell identified in step (d) having said morphological abnormality, wherein said chromosomal abnormality indicates that said cell is a transitional cell carcinoma (TCC) cell, wherein presence of said morphological abnormality and said chromosomal abnormality in the same said single cell confirms that said same single cell is a transitional cell carcinoma (TCC) cell;
- wherein said presence of said transitional cell carcinoma cell in said voided urine sample is indicative of a positive bladder cancer diagnosis.

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74-81. (Cancelled)

82. (Previously presented) The method of claim 72, wherein the transitional cell carcinoma cells are from a bladder cancer or a kidney cancer.

83. (Cancelled)

84. (Previously Presented) The method of claim 72, wherein said imaging is effected using an automated cell imaging device capable of at least dual imaging.

85. (Cancelled)

86. (Cancelled)

87. (Currently amended) The method of claim 72, wherein step (c) further comprising analyzing said transitional epithelial cells for a ~~wherein said morphological abnormality selected from the group consisting of~~ is an enlarged nucleus, ~~a high nucleus to cytoplasm (N/C) ratio~~, a considerable dark appearance of a cell ~~or-and~~ an irregular nuclear border as compared to a transitional epithelial cell with a normal morphology.

88. (Cancelled)

89. (Previously presented) The method of claim 72, wherein said chromosomal abnormality is a polyploidy of a chromosome selected from the group consisting of chromosome 3, chromosome 7 and chromosome 17.

90. (Cancelled)

91. (Previously presented) The method of claim 72, wherein said chromosomal abnormality is a loss of the 9p21 locus.